

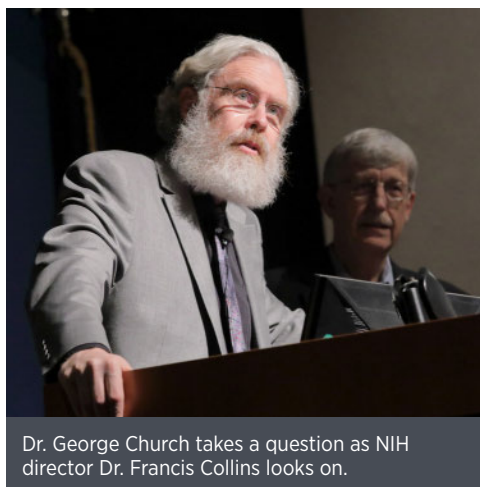


## Church Describes Medical Potential of Gene Editing

BY DANA TALESNIK

The thought of transplanting animal organs into humans conjures up images of the chimera—the Greek mythological monster with a lion’s head and a goat’s body. While this extreme is a long way off, rapid progress in gene-editing techniques at the heart of realizing such a transplant hold promise for developing new diagnostics and therapies in the next few years.

Recently, genome sequencing and gene-editing techniques have become faster, more accurate and cheaper thanks to the innovations of investigators such as Dr. George Church, who recently delivered



Dr. George Church takes a question as NIH director Dr. Francis Collins looks on.

the Marshall Nirenberg Lecture in Masur Auditorium.

“The thing that’s significant here is that we’re not just reading genes and their 64 types of triplet codons, which comprise the genetic code, but we’re also now writing

them and can do radical recoding,” said Church, professor of genetics, health sciences and technology at Harvard University and director, Harvard-NHGRI Center of Excellence in Genomic Science.

The ability to alter genes offers the potential to treat heart and organ failure, cancer and many inherited conditions. The reason it’s possible to read whole genomes and write them on the billion base pair scale is due to such gene-editing tools as CRISPR—a tool Church’s lab helped invent that can delete, insert or alter genes—and novel sequencing methods such as fluorescent *in situ* RNA sequencing.

Another integral part of Church’s research is engineering cells to make them resistant to viruses. “It’s interesting, both practically and philosophically—you can make an organism resistant to all viruses in the world, even viruses you’ve never studied

SEE **GENE EDITING**, PAGE 6

## ‘A THREAD TO PULL ON’

## Faster Sequencing, More Patients Boost Autism Research

BY RICH MCMANUS

A philanthropist’s largesse and faster sequencing technology are helping researchers gain footholds in understanding autism spectrum disorder, which affects between 1 and 2 percent of the population.

But complex diseases of brain and behavior such as ASD will not yield soon to simple solutions, said Dr. Matthew State, chair of the department of psychiatry at the University of California, San Francisco, School of Medicine.

ASD is “a tremendously heterogeneous disorder,” he said at a recent NHGRI intra-mural seminar in Lipsett Amphitheater. “Anyone who comes to us and says that 10 out of 10 autism patients have the same marker for idiopathic disease is [likely misguided].”

SEE **AUTISM**, PAGE 4



Debra Chew (l) of EDI and Dr. Hannah Valentine discuss models of diversity.

## GUIDED BY SOCIAL SCIENCE

## Business Model of Diversity, Inclusion Promoted

BY CARLA GARNETT

The idea of diversity has inspired a lot of metaphors for appreciating our differences: Distinctive flavors infusing a melting pot. Melodious voices singing in harmony. Multiple threads forming a tapestry. To be sure, the language brings to mind pleasant

SEE **DIVERSITY**, PAGE 8



Congressional delegation visits. See story, p. 12.

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## Pi Day Events Include Lecture by MIT's Berger, Mar. 14 in Porter Bldg.

NIH will mark the occasion of Pi Day, Tuesday, Mar. 14, with a series of events celebrating the intersection between the quantitative and biomedical sciences. Pi Day is an annual international celebration of the irrational number Pi, 3.141592...



MIT's Dr. Bonnie Berger is guest speaker at Pi Day.

A highlight will be a lecture by Dr. Bonnie Berger, Massachusetts Institute of Technology, titled "Mathematics of Biomedical Data Science," from 1 to 2 p.m. in Rm. 620/630 of the Porter Bldg. The last two decades have seen an exponential increase in genomic and biomedical data, which are outstripping advances in computing power. Extracting new science from

these massive datasets will require not only faster computers; it will require algorithms that scale sublinearly in the size of the datasets.

Berger is the Simons professor of mathematics at MIT with a joint appointment in computer science. After beginning her career working in algorithms at MIT, she was one of the pioneer researchers in computational biology and, together with the many students she has mentored, has been instrumental in defining the field. She continues to lead efforts to design algorithms to gain biological insights from recent advances in automated data collection and the subsequent large data sets drawn from them. She has received numerous honors, including election to the American Academy of Arts and Sciences.

View the full NIH Pi Day program at <https://nihpi-day.nih.gov/index.html>.

## Management Intern Program Unlocks New Career Paths

Have you heard of the NIH Management Intern (MI) Program? This is a highly competitive, 2-year career-development program for current NIH employees. MIs come from a variety of job backgrounds, including both scientific and administrative fields. Recent MIs have joined the program from positions as diverse as intramural program specialist, police officer, contract specialist, high-voltage electrician and extramural support assistant.

MIs rotate through different administrative career fields to gain invaluable insight into NIH while contributing to the work of the agency through

targeted assignments and challenging projects. After 2 years and upon completion of the program, MIs transition into an administrative-management career in one of many areas throughout NIH.

Although the hiring freeze has also frozen recruitment of MIs, you can learn more about the program, including how to contact MI program staff or current MIs or hear about future program dates by visiting <https://trainingcenter.nih.gov/intern/mi/>.

## FAES Announces Endocrinology Course

The Foundation for Advanced Education in the Sciences at NIH is holding its 2017 Endocrinology Review and Update Course Sept. 11-15. The course will prepare participants for the American Board of Internal Medicine endocrinology certification and recertification examinations.

The class will provide details on how to evaluate and apply new treatments in the diagnosis of endocrine disorders and to identify the risks and benefits of each treatment. The course will provide case studies as examples of examination questions. Participants will learn cost-effective approaches to clinical, laboratory and radiologic diagnosis of endocrine disease with emphasis on recent advances.

The week-long review will cover presentations and problem sets from experts in the field. Speakers include Dr. Francesco Celi of VCU Medical Center, Dr. Beverly Biller of Harvard Medical School and Massachusetts General Hospital, Dr. Electron Kebebew of NCI and Dr. Kristina Rother and Dr. Lee Weinstein, both of NIDDK.

Participants can earn up to 37 CME (continuing medical education) credits. Registration is required. Visit <https://faes.org/events/endocrinology-board-review-and-update-course-2017>.

## New Members of NLM Board of Regents

The National Library of Medicine board of regents welcomed three new members at its recent meeting. They are:

Jane Blumenthal, associate university librarian for health sciences and director of the Taubman Health Sciences Library at the University of Michigan. A past president of the Medical Library Association, she has more than 30 years of experience in information and library services.

Dr. Eric Horvitz, managing director and technical fellow at Microsoft Research. His research focuses on principles of machine intelligence and leveraging the complementarities of human and machine reasoning.

Dr. Gary Puckrein, executive director of the National Minority Quality Forum in Washington, D.C., which strengthens efforts to use evidence-based, data-driven initiatives to eliminate premature death and preventable illness for racial and ethnic minorities and other special populations. He created and launched *Minority Health Today*, which served clinicians practicing in minority communities.



NLM director Dr. Patricia Flatley Brennan (c) and Surgeon General Vivek Murthy (second from l) welcome new board of regents members (from l) Dr. Eric Horvitz, Jane Blumenthal and Dr. Gary Puckrein.

## 'Persisters' May Hold Clues to New Antibiotics

It was hard, on Feb. 15 at the Wednesday Afternoon Lecture, to determine what was more unexpected: A man named Dr. Kim Lewis, who spoke with a Russian accent (he grew up in Moscow); his discussion of "the paradox of chronic infections—antibiotics are ineffective against antibiotic-susceptible pathogens"; or a key realization that is enabling Lewis and his colleagues at Northeastern University's Antimicrobial Discovery Center to find new antibiotics worthy of succeeding the played-out warriors of the Golden Era of antibiotic discovery from 1930 to the early 1960s.

Lewis put the realization this way: "When Mother Nature comes up with a perfect defense [he was referring to so-called persisters—quiescent bacterial cells that survive lethal antibiotics or stresses but are capable of growing again under the right conditions], what we know is that it also provides a response to that perfect defense."

Lewis and his team have identified two compounds targeting the "Achilles heel of persisters"—lassomycin (so-named because, chemically, it resembles a lasso) and acyldepsipeptide, which has proven effective in mouse models of infection.

He feels sure there are other anti-persister compounds awaiting discovery.

Persisters were first named in 1944 by Dr. Joseph W. Bigger, who published his definition in *The Lancet* that year; the



Dr. Kim Lewis's lab has developed approaches for killing persister cells and growing uncultured bacteria. The lab found that this "microbial dark matter" harbors novel antimicrobials that evolved to be essentially free of resistance.

phenomenon was actually discovered by Gladys Hobby in 1942, when she found that penicillin could kill 99 percent of a streptococcal culture, leaving 1 percent intact. "And then [persisters were] largely forgotten for a couple of decades," said Lewis.


But the current resistance crisis in medicine, especially in *Klebsiella* infection and MRSA, is prompting an urgent worldwide search for new antibiotics. As Lewis observed, "You can't do effective surgery or chemotherapy without antibiotics."

He and his collaborators set out to characterize persisters and found a general mechanism. He observed, whimsically, "It's a pretty simple explanation—we could

have found this 10 years ago, but didn't, for reasons that I do not understand."

Just as bacteria have evolved a plurality of mechanisms for resisting antibiotics (remember that the original Cold War began when living cells, regarding each neighbor with suspicion, evolved ways of defending themselves), the paths to persistence are likewise multiple and redundant, Lewis said.

He called the realm of uncultured cells "microbial dark matter." And just as dark matter, in physics, must surely explain the universe's "missing mass" problem, so too may further investigations of uncultured cells yield new medicines that can kill the bad guys and preserve the good ones.

The full talk is available at <https://videocast.nih.gov/summary.asp?Live=21817&bhcp=1>. —Rich McManus 



ON THE COVER: Crab apple tree flowers at NIH

IMAGE: SOMA CHOWDHURY

### The NIH Record

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On the day after his WALs lecture, Lewis was a guest at the NIH Lambda Lunch meeting in Bldg. 37, where he spoke on "Stochastic changes in energy levels produce drug-tolerant persister cells." His hosts included Dr. Susan Gottesman (l) and Dr. Gisela Storz.

PHOTOS: ERNIE BRANSON

**NIH** National Institutes of Health  
Turning Discovery Into Health



Dr. Matthew State of UCSF spoke on genetic studies of autism spectrum disorder.

## Autism

CONTINUED FROM PAGE 1

Genetic surveys of the cause of ASD began to be successful in the early 2000s, he said, with research groups now converging on roughly the same set of genes during the past decade. Some 65 ASD-associated genes have been identified so far, said State, with scientists having the highest confidence in about 30 of them.

"We expect the final number will be somewhere between 400 and 1,000," he said.

It has long been known that genes play a major role in ASD, a broad set of disorders of social communication, but State said there are no treatments that are highly effective, particularly for the core social deficits. "The mainstay, first-line treatment is behavioral therapy," he noted. "But our lack of knowledge about the molecular, cellular and circuit mechanisms in ASD is profoundly limiting."

Abetting the search for those mechanisms are whole-exome studies of simplex families, those in which there is a single affected child, where both parents and other offspring are normal. The Simons Simplex Collection, a data bank of information on 3,000 ASD families, has given researchers "a thread to pull on," said State.

New York philanthropist Jim Simons funded the collection, inspired by advances made by the Cold Spring Harbor laboratory of Dr. Michael Wigler in 2007 that were

later underscored by State and colleagues and other labs, including Wigler's, in larger patient cohorts.

"Advances in autism research tend to come in waves, of both technological advances and more participants," State said.

A 2011 microarray study involving about 1,000 simplex families detected a higher percentage of copy number variations in those with idiopathic autism. De novo mutations were found in both affected and healthy family members, however, and involved both deletions and duplications, State said. Scientists, however, were able to use the observation that these rare mutations hit the same gene or region in those affected to find the specific genetic contributors to ASD.

So far, ASD genes appear to function largely in two domains, chromatin modification and synaptic structure and function, said State.

"For the first 15 years of my two decades in this field, we were wandering in the desert," he explained. "It's only in the last 5 years that we've really begun to get a glimpse of the Promised Land."

A practicing child psychiatrist, State said he "cares most about pathophysiology, not just biology." His goal is to develop new treatments that help families and individuals.

It is known that advanced paternal age is associated with greater risk of ASD, only in part due to gene-disruptive single-nucleotide variants. And girls with ASD have a greater burden of mutations, suggesting that somehow their biology protects them against ASD.

State said that whole-genome sequencing is a popular new tool in ASD studies, but he thinks it is under-powered at present for gene discovery.

"Everyone's surfen' now, and we are too," he said. "But this ain't gonna be easy."

The power issue—how many samples are needed to see an unmistakable signal—is a challenge in ASD research. As these samples get much larger, whole genome sequencing

★ ★ ★

*"For the first 15 years of my two decades in this field, we were wandering in the desert. It's only in the last 5 years that we've really begun to get a glimpse of the Promised Land."*

—DR. MATTHEW STATE

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will almost certainly play an increasingly important role.

In addition, State predicts that drop-seq, a technology that allows biologists to analyze genome-wide gene expression in thousands of individual cells in a single experiment, "will help us interpret the genes we have found. It will explode our concept of how many cells there really are in the brain."

He and his colleagues are also pursuing a spatio-temporal approach to the developing brain, to find out when and where ASD genes do their damage. Initial forays taking this approach have pointed to deep-layer cortical glutamatergic neurons in the fetal cortex.

"The BRAIN initiative's goal of a complete census of brain cells would be very helpful," he noted.

State concluded by predicting "a new era in the study of developmental neuropsychiatric disorders." Stay tuned. **R**



## Allen Named NIMHD Executive Officer

Kimberly Allen recently was named executive officer at the National Institute on Minority Health and Health Disparities. She had served as deputy EO since 2015. Before coming to NIMHD, Allen was deputy executive officer at NIGMS. She will serve as principal advisor to the director on management issues affecting the institute and will continue to serve as a key member of the leadership group in executing the strategic mission.

## Chronic Sleep Deficiency Can Lead to Long-Term Health Problems

BY ERIC BOCK

Not getting enough good quality sleep on a regular schedule does much more than make you sleepy. Over the course of a lifetime, sleep deprivation affects your heart, immune system and emotional well-being, said Dr. Michael Twery at a lecture on Feb. 6 in Bldg. 45.

“Our bodies have evolved to provide the chemistries that support life during the daytime to help us deal with stress during the day and to repair and recover at night,” said Twery, director of NHLBI’s National Center on Sleep Disorders and Research.

Most adults need 7-8 hours of sleep per night. However, the exact amount and schedule for sleep can vary from person to person, he said. When a person goes to bed, a biological process sometimes referred to as circadian rhythm unfolds. This biological clock ticks in any cell with a nucleus—it’s present in everything from microbes to plants to humans.

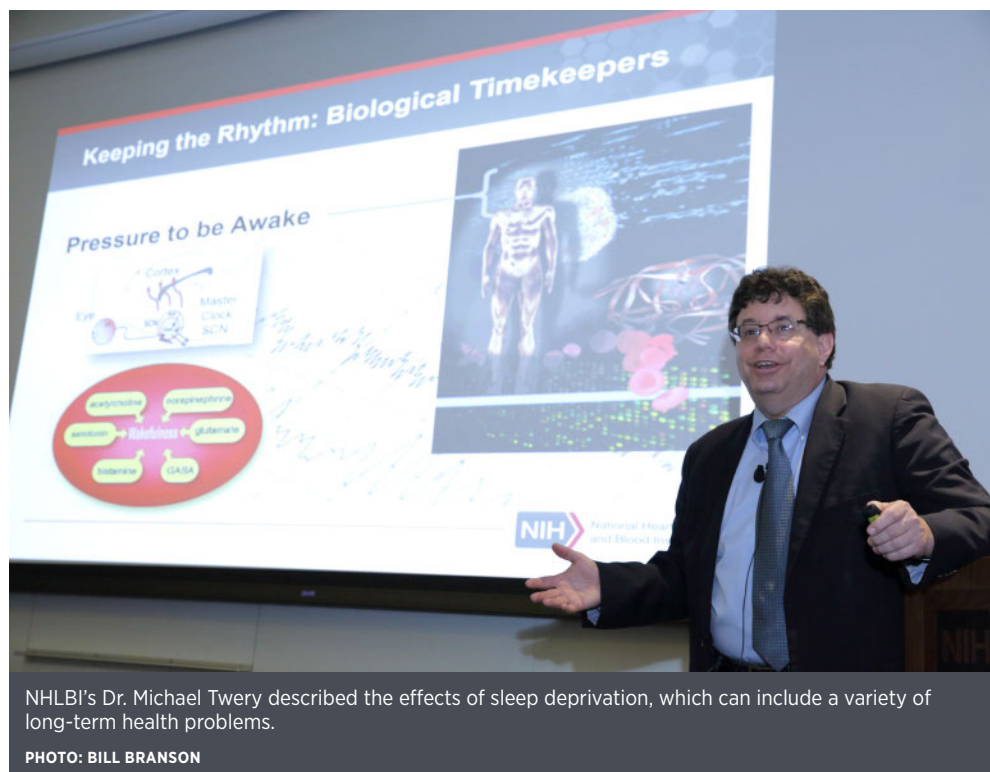
“It’s controlling our proteins, our genes and the metabolism of cells. And it’s affecting disease pathogenesis,” he explained.

Although it’s unclear exactly why this process happens, evolutionary biologists suspect the circadian clock synchronizes with the availability of light. During the day, a person’s retina detects light and signals the brain that it’s daytime. Eating and exercising also let the brain know when to be awake. At the same time, Twery explained, a person accumulates a neurotransmitter called adenosine while awake. As adenosine levels rise, the urge to sleep increases.

“The urge for sleep is low in the morning and there’s a little bump in the afternoon. And then it goes up again at night, when we want to go to sleep,” Twery said.

Once a person falls asleep, several chemical reactions occur. Some, for example, stimulate the production of hormones that help cells and DNA repair themselves while others help control the body’s use of energy. Skin cells and intestine cells proliferate.

“When we start to deprive ourselves of sleep, it’s not just a matter of less sleep. We don’t complete the pattern. We don’t get all the cycles of sleep. And we don’t secrete the



NHLBI's Dr. Michael Twery described the effects of sleep deprivation, which can include a variety of long-term health problems.

PHOTO: BILL BRANSON

hormones,” he observed. “This snowballs into disease and metabolic problems.”

Staying up late once in a while won’t hurt, but staying up late, getting up early frequently and irregular sleep schedules cause problems. Those who regularly stay up late and wake early are susceptible to heart ailments such as atherosclerosis, coronary heart disease and weakening of the heart muscle. Not enough rest affects the heart’s ability to pump blood and makes it work harder.

Those who are well-rested are motivated, more inspired, have better memories and are able to better regulate their emotions. Sleep-deprived spouses, for instance, might have trouble communicating with each other or their children. Driving a car while drowsy can be very dangerous. Students who sleep through class typically don’t do well in school. Not getting enough sleep “drags everything down.”

Twery warned that naps aren’t a substitute for getting enough sleep at night. While they can remedy the feeling of sleepiness, naps don’t protect a person’s health since they do not support the rhythm of circadian function. The immune system doesn’t get the opportunity to repair itself. Those who are tired may also eat more because food replenishes our emotional reserves.

To get a better night’s sleep, Twery suggested avoiding stimulants such as caffeine and screen time late in the day, taking part in calming activities at night and using as little light as possible before going to bed in a cool, dark and quiet room. There are caveats, though.

“Your vulnerability to artificial light at night—like TV sets and tablets—hinges in part on how much light you get during the day,” he said.

For those who can’t sleep, he advises keeping a sleep diary that can be shared with a physician who can analyze the problem.

Getting enough sleep at night and light during the day is just one component of wellness. People also need to eat a balanced diet and exercise regularly. “All of these activities are tied together,” Twery noted. “You can’t separate them and maintain your health.”

The talk, part of the “Focus on You” series, was sponsored by the Office of Research Services’ Division of Amenities and Transportation Services in partnership with the NIH Health and Wellness Council and NHLBI. It can be seen at <https://videocast.nih.gov/Summary.asp?File=21123&bhcp=1>. **R**



Collins, Church and NHGRI director Dr. Eric Green confer in Masur Auditorium prior to Church's recent WALS lecture.

PHOTOS: ERNIE BRANSON

## Gene Editing

CONTINUED FROM PAGE 1

before, because they all expect a genetic code to be provided by the host, and we can change that radically without impacting the host," he said.

All genetic organisms share a similar, though not identical, genetic code and all, so far, use all 64 codons (three base pairs of A, C, G, U that correspond to one of 20

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*"Many of the technologies I've brought up raise issues."*

-DR. GEORGE CHURCH

• • •

specific amino acids) in some way. "We were surprised," Church said, "that even changing one codon type was enough to make it resistant to most classes of viruses."

Church's lab is part of NIH's BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative that seeks to analyze brain function with the goal of treating and preventing brain disorders. Astonishingly, Church and colleagues are also busy editing genetic code with the goal of building brains.

"We're not just interested in making brains," said Church. "We also want to make sure that when we make these organoids, they are physiologically reasonable and, if they're not, we want to debug them with all the tools that we have."

The idea of genetically modified humans may seem frightening, but as Church pointed out, there already are tens of thousands of them out there thanks to recent research trials for gene therapy.

"Many of the technologies I've brought up raise issues," said Church. "We have a special responsibility to point out the downsides and the solutions to the downsides and then the

problems that the solutions create, and further tweaks, which makes people nervous, but we need to do it."

Gene therapy also holds the potential to alleviate sperm infertility, via stem cell clones, said Church. And, editing recessive genes may prevent early onset of genetic diseases such as Tay-Sachs.

"The irony is that germline therapy might reduce embryo harm rather than increase

it," said Church. "So we need to not be too dismissive and think carefully about this."

Also foreboding to some is the idea of altering behavioral and cognitive traits. But altering genes can potentially be used to prevent Alzheimer's and various disabilities, Church said.

Another type of genome engineering, RNA-guided gene drives, is under testing for controlling vector-borne disease. This could have global public health implications, particularly in developing countries that

cannot afford medicines or easily distribute them in remote areas. Church's lab has begun some experiments using CRISPR in malarial mosquitoes and to immunize animal reservoirs.

Dozens of gene therapies are now in veterinary clinical trials that could lead to human therapeutics, said Church. Pigs would be model candidates as their organs most closely resemble the shape and size of human organs. But a longstanding concern has been the potential for human recipients to contract porcine endogenous retroviruses (PERVs). Church's lab, using CRISPR on these genes in 14 days, knocked out 62 PERVs at once—followed now by 45 genes involved in immune rejection and clotting.

With progress in gene therapy comes a host of biosafety, ethical and legal concerns. As these issues are debated, the words of the late Nobel laureate Dr. Marshall Nirenberg still ring true. In a 1967 editorial published in *Science*, he wrote: "When man becomes capable of instructing his own cells, he must refrain from doing so until he has sufficient wisdom to use this knowledge for the benefit of mankind." **R**

## Avenevoli Named NIMH Deputy Director



Dr. Shelli Avenevoli

Dr. Shelli Avenevoli has been named deputy director of NIMH. She steps into the post having served as acting deputy during NIMH's search for a new permanent director. She brings to the role a background and research interest in developmental science and epidemiology and a record of leadership within NIMH and in numerous cross-institute and interagency scientific collaborations.

Avenevoli came to NIH in 2001, joining the NIMH intramural research program as a staff scientist. Among the studies in which she was a co-investigator was the National Comorbidity Survey-Adolescent Study, which aimed to gather information about the prevalence and course of mental disorders in children and adolescents. She moved to NIMH's extramural program in 2005, ultimately becoming chief of the Developmental Trajectories of Mental Disorders Branch. While there, she guided the reorienting of NIMH's translational neurodevelopmental research portfolio towards an emphasis on etiology, brain development and neurobiological function. She also led the building of a research program aimed at bipolar disorder and early, chronic irritability in children.

She has played a leadership role in a long list of collaborative initiatives and reports focusing on development. Most recently, she represented NIMH on the planning committees for the Environmental influences on Child Health Outcomes study and the Adolescent Brain Cognitive Development study.

As acting deputy director, she helped revise and implement NIMH's strategic plan and the institute's process for evaluating and approving funding opportunity announcements. Of the latter, former acting NIMH director Dr. Bruce Cuthbert said, "The revised process involved more staff members in the initiation and decision stages and resulted in better-targeted funding announcements." He praised Avenevoli's "thoughtfulness and her ability to quickly distill major points and identify issues. She played a leadership role in the task of revising NIMH's funding announcements for clinical trials, including introducing different announcements for pharmaceutical, behavioral and device-oriented trials to help investigators develop optimal trial designs."

Prior to joining NIMH, Avenevoli received her Ph.D. in developmental psychology from Temple University and completed an NIMH-funded postdoctoral fellowship at Yale.

NIMH director Dr. Joshua Gordon expressed his appreciation for what she brings to the post: "It is incredibly helpful—and a great pleasure—to have someone with Dr. Avenevoli's insight and experience in the deputy role during a period of transition for me and for NIMH."—**Charlotte Armstrong**

## Mixed Results for Trials of Testosterone in Older Men

In older men with low testosterone, 1 year of testosterone treatment improved bone density and corrected anemia of both known and unknown causes, but also increased the volume of coronary artery plaque, according to results reported from the Testosterone Trials (T Trials). Testosterone treatment had no effect on memory or other cognitive function. The results were reported in two journals of the American Medical Association.

The T Trials were conducted at 12 sites across the country in 790 men age 65 and older with low levels of testosterone and symptoms to which low testosterone might contribute. The studies were funded primarily by NIA; NHLBI, NINDS and NICHD also contributed. Additional funding, and the study drug and placebo, were provided by AbbVie Pharmaceuticals.

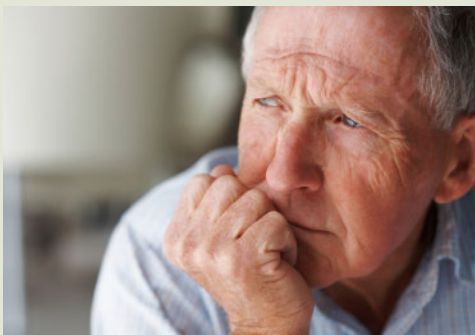
"A number of older men have testosterone levels below those found in healthy younger men," said NIA director Dr. Richard Hodes. "In most cases, these low levels are not due to diseases known to affect testosterone levels. Many of these men also have problems that could be related to low testosterone, including impaired cognition, anemia, cardiovascular disease, diminished sexual function, decreased mobility and fatigue. The T Trials were designed to determine if testosterone treatment might help alleviate these symptoms and conditions while monitoring for adverse effects."

"The results on diverse outcomes indicate the potential trade-offs between benefits and risks of testosterone treatment in older men," said Dr. Evan Hadley, director of NIA's Division of Geriatrics and Clinical Gerontology. "However, clarifying the effects of testosterone on many major clinical outcomes such as cardiovascular events, fractures and disability will require longer, larger scale trials. The results also illustrate that decisions about testosterone treatment need to be individualized, taking into account each patient's balance of risks for the various conditions that testosterone treatment could affect."

## Survival Rate Seen Improving For Extremely Preterm Infants

Very early preterm infants are more likely to survive than in previous years and the survivors are less likely to have neurological problems, according to an analysis of records from an NIH research network.

Researchers found that of the more than 4,000 infants born at 11 sites within the network from 2000 to 2011, survival rates increased from 30 percent to 36 percent. The proportion of survivors who did not have a neurological or developmental impairment increased from 16 percent to 20 percent. The authors theorize that



**T Trials' mixed results.** In older men with low testosterone, 1 year of testosterone treatment improved bone density and corrected anemia of both known and unknown causes, but also increased the volume of coronary artery plaque.

these improvements are a result of advances in the care provided to expectant mothers and their newborns.

The study appeared in the *New England Journal of Medicine*.

"Our study provides important information for physicians and family members planning the care of these extremely fragile newborns," said study author Dr. Rosemary Higgins, a program scientist at NICHD. The study was conducted by researchers in the NICHD-funded Neonatal Research Network.

Infants in the study were born between the 22nd and 24th week of pregnancy, far earlier than the 40 weeks generally expected for a pregnancy to reach term. Those born from 2008 to 2011 had the lowest death rate (64 percent). From 2004 to 2007, the death rate was 70 percent, unchanged from 2000 to 2003.

Higgins stressed that the results encompass trends for a large number of infants at multiple research sites, but they should not be used to predict the outcome for an individual child.

"Every individual is different, and no single source



Very early preterm infants are more likely to survive than in previous years and survivors are less likely to have neurological problems, according to an NIH research network analysis.

of information can precisely predict a baby's chances of survival or disability," she said. "But our study's findings do provide important information that physicians and family members can consult to help determine treatment strategies."

Providing care to infants born so early is often challenging. Physicians and family members can be reluctant to expose an infant to sometimes painful life-support procedures. Those offered active treatment may survive, but may have hearing loss, blindness, cerebral palsy and severe intellectual disability.

## Experimental Malaria Vaccine Provides Protection Against Multiple Strains

An investigational malaria vaccine has protected a small number of healthy U.S. adults from infection with a malaria strain different from that contained in the vaccine, according to a study published Feb. 21 in the *Proceedings of the National Academy of Sciences*. NIAID sponsored and co-conducted the phase 1 clinical trial.

Malaria is transmitted to humans through the bite of infected mosquitoes, which inject immature malaria parasites called sporozoites into a person's bloodstream. The parasites travel to the liver, where they mature, multiply and spread via the bloodstream throughout the body causing malaria symptoms including chills, fever, headache, nausea, sweating and fatigue.

According to the World Health Organization, 214 million people were infected with malaria globally in 2015 and 438,000 people died, mostly young African children. The species *Plasmodium falciparum* is the most common cause of malaria morbidity and mortality in Africa. In the United States, travel-related malaria is a concern for international tourists, aid workers and military personnel worldwide.

The PfSPZ vaccine used in this study was developed by Sanaria Inc., of Rockville. It contains weakened *P. falciparum* sporozoites that do not cause infection but are able to generate a protective immune response against live malaria infection. Earlier research at the Clinical Center with the vaccine found it to be safe, well-tolerated and protective for more than a year when tested in healthy U.S. adults against a single Africa-derived malaria strain matched to the PfSPZ vaccine.

"An effective malaria vaccine will need to protect people living in endemic areas against multiple strains of the mosquito-borne disease," said NIAID director Dr. Anthony Fauci. "These new findings showing cross-protection with the PfSPZ vaccine suggest that it may be able to accomplish this goal."



Bonita White of HHS outlines ERG Community of Practice ground rules.

## Diversity

CONTINUED FROM PAGE 1

images and offers novel ways of looking at employing all of our differences toward the greater good.

These days, though, the workforce marketplace has shifted toward a business view of diversity: How can we use it to achieve our best bottom line? One strategy is—establish an employee resource group (ERG) Community of Practice.

Already in widespread use in many corporate settings, the Community of Practice philosophy—as its name suggests—focuses on engaging employees first, putting workers in a position to advance the collective mission by simultaneously moving their own group and individual interests forward.

Large agencies such as NIH can have as

many as 20 or 30 different ERGs tailored to address the unique needs involving employees' race, nationality, color, gender and disability. For example, Federally Employed Women, Blacks In Government, Deaf Employees Advisory Forum, the Asian and Pacific Islander American Organization and Salutaris have all established homes at NIH over the years.

The NIH Office of Equity, Diversity and Inclusion, which welcomes and helps all such organizations as part of its mission, and the NIH chief officer for scientific workforce diversity (COSWD) want to bring all ERGs together to form a Community of Practice. The strategy encourages groups to consider

various employee special emphasis organizations that exist across NIH. Our move to develop a Community of Practice will be no different in that sense—we'll continue to provide the same strong, consistent support to those groups."

A Community, however, can benefit both NIH and individual organizations in ways the groups can't achieve alone. Communities of Practice help with recruitment, for instance, by broadening an agency's applicant pool. Employee retention also stands to gain through development of an effective Community by providing a consistent, stable environment experienced in handling diverse issues.



*"Adopting the Community framework simply raises our role to a new level. It allows NIH as an agency both to keep pace with other federal and corporate organizations and—depending on how we structure our ERG—to move ahead of the field."*

—DEBRA CHEW



a broader purpose—helping NIH achieve its mission through strategy.

"There's a wealth of knowledge and talent within the NIH ERGs and we wish to serve as conduits to expose the diverse thoughts, ideas and talent for the greater good," explained Debra Chew, EDI director. "Traditionally, EDI—and its predecessor offices—have always developed creative and successful ways of supporting the

Workers who have adopted the Community concept also report feeling better connected to their organization's leadership and experiencing more ways to network and mentor, said Kay Johnson Graham, a strategist in the EDI Diversity and Inclusion Branch familiar with recent social science research results on ERG Communities.

"If you want to have a real impact," she said, "then align groups of people who are interested in diversity with the strategies and mission-related work of your organization."

"Career development will also be an important component of Community development," explained Ashley Wells, a strategist in EDI's Special Emphasis Portfolio Branch. That's just one of the incentives ERG Communities offer to engage employees, she said.

"ERG Communities are really becoming the new training ground for grooming talent," Graham added. "We're looking at establishing new leadership opportunities and better succession planning."

At an inaugural meeting to consider the idea a few months ago, EDI hosted



Representatives from about 20 different NIH ERGs attend the inaugural Community meeting, along with EDI staffers, NIH chief officer for scientific workforce diversity Valentine and EDI director Chew.

PHOTOS: ASHLEY WELLS

guest presenters Bonita White of HHS and Nicole Lassiter of OPM to discuss ways NIH can adopt the Community model. Representatives from about 20 different NIH ERGs attended, along with Chew and Dr. Hannah Valantine, NIH chief officer for scientific workforce diversity.

“Employee resource groups are vital for our success, since not only do they support community discussion, but also they help connect diverse talent with new scientific opportunities at NIH,” said Valantine.

EDI and COSWD hope to be the bridge between the agency’s burgeoning ERG Community and NIH leadership.

“Adopting the Community framework simply raises our role to a new level,” Chew continued. “It allows NIH as an agency both to keep pace with other federal and corporate organizations and—depending on how we structure our ERG—to move ahead of the field. [The private sector and a few other government agencies] may have a couple of years’ head start on us, but with efficient and effective planning, we can surge ahead on this.”

Currently, EDI is working on the next steps in such a plan. Following the initial meet-and-greet event at which White outlined ERG ground rules and Lassiter discussed best practices, EDI’s Division of Diversity and Inclusion began laying the foundation for forming a Community here to share promising practices in the field and provide support to the ERGs.

One big challenge, they acknowledge, will be buy-in from NIH entities familiar with previous models of employee engagement. But if the success of the first meeting is any indication, most NIH’ers will be eager to be in on the ground floor of a new venture that they can help design.

The next gathering is also in the works, as strategists try to capitalize on the momentum and enthusiasm the inaugural meeting generated.

“The field is changing a lot,” concluded Graham, “and in order to be competitive in attracting and keeping the highest quality workforce, we have to change as well.” **R**

## ORWH DIRECTOR HONORED

### Awards to Clayton Highlight Interest in SABV

For the past couple of years, Dr. Janine Austin Clayton, director of the Office of Research on Women’s Health, has spearheaded efforts to shape and implement a new policy for NIH-funded research: sex as a biological variable, or SABV.

Established in 2015, the SABV policy requires NIH-funded researchers to factor sex into the design of studies involving vertebrate animals and humans, as well as the analysis and reporting of research results. The goal is to identify and understand influences SABV might have on health and disease by ensuring that women and female animal models are as appropriately studied as men and male animal models. Such efforts may help ensure that women receive the most optimal care.

Clayton’s efforts have not gone unnoticed. Recently, she received two awards: the Red Dress Award from *Women’s Day* magazine, a general audience publication with more than 16 million subscribers that focuses on concerns important to women, and the Dr. Nathan Davis Award from the American Medical Association, an organization that since 1847 has played a critical role in the development of medicine in the United States.

Clayton received the Red Dress Award at the 14th annual Red Dress event in New York City on Feb. 7. In presenting the award, *Woman’s Day* recognized Clayton’s work in combating heart disease—the number-one killer of women—and her exploration of sex and gender in health, noting that her work could help foster new discoveries that directly benefit the health of women.

The AMA also recognized Clayton’s work in accounting for sex and gender in biomedical research, presenting her with the Dr. Nathan Davis Award at an event held in Washington, D.C., on Feb. 28. Named for the founder of the AMA, the award is considered one of the most prestigious honors recognizing the work of elected officials and career government employees. It highlights accomplishments that advance public health.

“The work that I am doing rests on a foundation established by many scientists, clinicians, health advocates and others who saw this critical gap in knowledge early and continue to help close it,” said Clayton. “It has been exciting to work in partnership with so many different stakeholders within NIH and its institutes and centers to show the value of SABV in the context of a diverse set of disciplines and scientific areas. I am particularly grateful to [NIH director] Dr. [Francis] Collins and other leaders within NIH for making SABV a priority.”

Clayton noted that the awards from *Woman’s Day* and the AMA demonstrate that many people—from laypersons to medical professionals—are recognizing the importance of sex, as well as gender, in research and medicine. She calls on every biomedical scientist to ask, “What role might sex/gender play in my area of research?”

ORWH has been conducting roadshows on SABV for NIH institutes and centers, complementing Clayton’s work on the trans-NIH SABV working group.

To receive a presentation on sex/gender and research, contact ORWH at [ORWHINFO@mail.nih.gov](mailto:ORWHINFO@mail.nih.gov). Frequently asked questions about SABV and how it helps support rigorous and transparent research can be found at <https://grants.nih.gov/reproducibility/faqs.htm>. —Marilyn Fenichel, Lamont Williams



ORWH director Dr. Janine Austin Clayton speaks at the Red Dress event in New York City.

PHOTO: RABBANI & SOLIMENE PHOTOGRAPHY



Dr. Steve Newell, Barbara Wojciechowski (c) and Dr. Carole Christian recently joined NIMHD.

## NIMHD Welcomes Three New Staffers

The Office of Strategic Planning, Legislation and Scientific Policy at the National Institute on Minority Health and Health Disparities has added three staffers.

Dr. Steve Newell works as a health scientist. He assists in coordinating trans-NIH activities, preparing reports to Congress and planning strategic priorities and policies.

Prior to joining NIH, Newell served as a science and technology policy fellow on behalf of the Society for the Psychological Study of Social Issues and the American Association for the Advancement of Science in the office of Sen. Bernie Sanders (I-VT).

Barbara Wojciechowski has joined the office as a statistician. She will be contributing to data analysis, data management, data mining, evaluation and assessments.

Before joining NIH, she served as a statistician for the Veterans Administration's Health Equities and Rural Outcomes Center of Innovation at the Ralph H. Johnson VAMC in Charleston, S.C.

Wojciechowski holds an M.A. in mathematics with an emphasis on statistics from the University of West Florida and an M.S. in biomedical sciences with an emphasis on epidemiology from the Medical University of South Carolina. She is a grandmother of two baby girls and loves to crochet in her free time.

Dr. Carole Christian works as a health science administrator. She comes to NIMHD from the Office of Portfolio Analysis in the Division of Program Coordination, Planning and Strategic Initiatives and has been with NIH for 9 years. In addition to performing portfolio analyses, she founded and co-chaired the portfolio analysis interest group and initiated the OPA blog. Christian also planned and implemented symposia and workshops for OPA.

Prior to NIH, she worked at the Department of Defense Congressionally Directed Medical Research Programs as a science officer. Christian received

her Ph.D. in virology at Johns Hopkins School of Public Health.



Dr. Hilary Sigmon

## CSR's Sigmon Says So Long, After 30 Years at NIH

BY PAULA WHITACRE

As a child in Bethlehem, Pa., Dr. Hilary Sigmon wanted to become a nurse. She did not envision then, however, that nursing would lead to master's and doctoral degrees and a research career. Sigmon retired recently after 30 years at NIH, the last 15 as a scientific review officer in the Center for Scientific Review.

Sigmon attended the University of Pennsylvania. "Penn had a 5-year program at the time where I could earn a B.A. in sociology and also a diploma from the Hospital of the University of Pennsylvania School of Nursing," she explained.

As a registered nurse, she moved to Washington, D.C., in 1973. She worked in George Washington

University Hospital's intensive care unit and later earned her master's degree in nursing from Catholic University. She became a clinical nurse specialist in the intensive care units at Johns Hopkins Hospital and research assistant in Hopkins' pathology department. She then moved to Washington Hospital Center to orchestrate the nursing flight team and co-head its shock trauma unit and helicopter emergency service.

Sigmon earned her Ph.D. at the Uniformed Services University of the Health Sciences in physiology, studying antithrombin III and its effect in disseminated anticoagulation during septic shock. "I defended my dissertation a month later than I planned because I gave birth to my son," she recalled.

Sigmon first came to NIH through the National Center for Nursing Research, now NINR. "They were looking for a nurse-physiologist to help build their basic science portfolio," she said. "It was a great entrée for a nurse researcher at the NIH," she said.

In 2000, she moved to CSR as SRO for the Fogarty International Center to conduct site visits to projects in Russia, Haiti, Uganda and China—all in 6 months. "I basically did not sleep," she said. Her

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*"The profession of nursing allowed me to fulfill my dreams. It took me to places I never imagined, including international research related to HIV/AIDS."*

-DR. HILARY SIGMON

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background helped her form teams with the right mix of expertise, she noted.

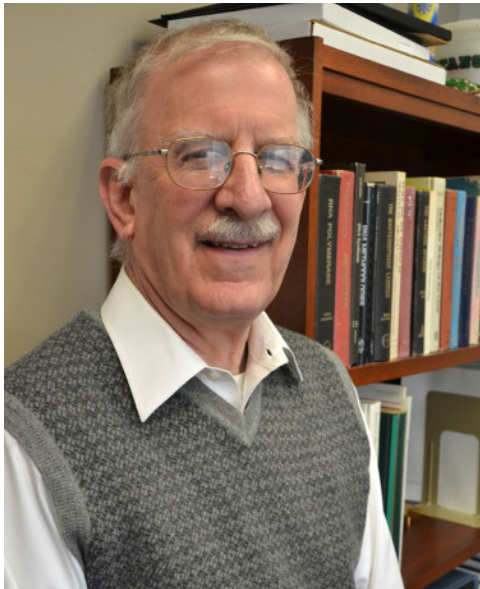
"Hilary changed the model of how international initiatives are reviewed at CSR," said Dr. René Etcheberrigaray, CSR deputy director. She involved a range of study sections, he explained, tapping into their scientific expertise while helping them understand the resource constraints in many middle- and low-income countries.

As another lasting contribution, Sigmon was SRO of the AIDS clinical studies and epidemiology study section. "She was part of the group of people who made a big difference in HIV/AIDS going from an acute disease that killed people to a chronic disease," said Dr. Robert Freund, chief of the AIDS and AIDS related research integrated review group. "Her dedication to patients and applicants moved the field forward."

In retirement, Sigmon divides her time between Maryland and Florida, travels internationally,

volunteers for political causes and takes Spanish classes.

She remains an active alumnus of Penn, which her husband, sons, sister and other family members also attended. She credits her R.N. training there as the beginning of a challenging, yet unexpected trajectory. "The profession of nursing allowed me to fulfill my dreams," she said. "It took me to places I never imagined, including international research related to HIV/AIDS."



Dr. Arnold Revzin

## Revzin Retires from CSR

BY PAULA WHITACRE

In an earlier stage in his career, Dr. Arnold Revzin pioneered the gel shift assay, a widely used method to determine if protein binds to a given DNA/RNA sequence. He transferred the creativity and perseverance that marked his research to the Center for Scientific Review, where he retired recently as chief of an oncology integrated review group.

Revzin's ability to "roll up his sleeves and get to work" distinguished him as an outstanding scientist, administrator and NIH colleague, said Dr. Donald Schneider, senior advisor to the CSR director and former director of CSR's Division of Basic and Integrative Biological Sciences. "We were lucky to have Arnold as a colleague. He has been a constructive force with substantial presence at NIH."

Revzin grew up in Chicago and majored in chemical engineering at the University of Michigan. "I gravitated to the 'chemical,' not the 'engineering' side," he said. He went on to the University of Wisconsin, where he received his Ph.D. in physical chemistry. He then conducted postdoctoral research at the Weizmann Institute, Max Planck Institute and University of Oregon.

He joined the Michigan State University faculty in

1975 and is now professor emeritus. In 1981, his co-authored article introducing the gel shift assay garnered some 900 citations; he has also published numerous other articles, monographs and chapters.

In 1984, a 1-year rotation appointment as a program director at the National Science Foundation proved pivotal in two ways. First, when he returned to MSU, he went into administration, becoming associate dean in the College of Natural Science and assistant vice president for research services. Second, he found he enjoyed working in a federal science agency.

When his wife took a position at the National Archives in Washington, Revzin sought a position at NIH. He joined CSR in 1998 as a scientific review officer for three biophysical chemistry study

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*"When I came to NIH, I found I enjoyed contributing to science in a different, broader way."*

-DR. ARNOLD REVZIN

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sections. He also worked as a referral officer to assign grant applications to study sections for peer review. In 2013, he became chief of the oncology 1-basic translational IRG.

Revzin took on other assignments while at CSR, including chairing committees on training and on scientific overlap to respond to appeals by grant applicants. He also enjoyed outreach opportunities, explaining the review process to postdocs and early stage investigators at scientific meetings.

"Arnold is the ultimate professional," said Dr. Noni Byrnes, current director of the Division of Basic and Integrative Biological Sciences. "He is easygoing, with a tremendous sense of integrity." Schneider said he appreciated Revzin's "ability to blend a blunt honesty with a wonderful sense of humor."

Looking back, Revzin enjoyed each aspect of his career. "I liked being a faculty member and administration was interesting because I wanted to see how the university worked," he said. "When I came to NIH, I found I enjoyed contributing to science in a different, broader way."

Revzin will continue to "roll up his sleeves" in retirement. He volunteers at an addiction treatment center associated with Suburban Hospital. By taking on some of the center's administrative and front-desk tasks, he frees up the professionals to focus on patient care. He also plays the recorder with a group of fellow musicians, mostly classical and occasionally ragtime and other genres of music. He also appreciates having more time to travel and to visit family members, including two grandchildren in Houston. **R**

## Study Seeks Healthy Older Adults

Healthy older adults, ages 55-70, are invited to participate in an outpatient research study investigating the benefits of tart cherry and aroniaberry supplementation on vascular health. The goal of the study is to determine whether the supplements improve blood flow and blood vessel function that can affect your heart. Eligible participants must be medication-free and in good general health. The study will be carried out in an outpatient clinic and includes 7 visits over 3-4 months. Compensation for the study is provided. For more information, call 1-800-411-1222 (TTY 1-866-411-1010) and refer to study 15-NR-0085 or visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

## People with Dry Mouth Needed

NIDCR is seeking people with dry mouth due to radiation therapy for head and neck cancer. Researchers are testing whether an investigational gene therapy using "AAV2hAQP1" increases saliva in patients who have received radiation therapy for head and neck cancer. Travel to and from the Clinical Center (within the U.S.) will be provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010). Read more online at <https://go.usa.gov/x8yXE>. Refer to study 15-D-0129.

## Study on Depression, Repeated Doses Of Ketamine Now Enrolling

Join a research study on depression. The purpose of the study is to evaluate the rapid and sustained antidepressant effects of repeat doses of ketamine in the brain. We want to learn how ketamine affects areas of the brain important in regulating mood and if there are unique signatures that could help predict who may respond to the drug. Also, we want to see if repeated doses of ketamine are safe and effective in treating the symptoms of depression. We are enrolling eligible adults, ages 18 to 65 with major depressive disorder. This inpatient study lasts 14-20 weeks. Procedures include a medication taper and drug-free period, taking repeated doses of the research drug, taking placebo, multiple brain imaging scans, transcranial magnetic stimulation and psychological testing. After completing the study, participants receive short-term follow-up care at NIH while transitioning back to a provider. There is no cost to participate. Compensation is provided. Study enrolls eligible participants from across the U.S. Travel arrangements are provided. Costs are covered by NIMH. To find out if you qualify, call 1-877-646-3644 (1-877-MIND-NIH) TTY 1-866-411-1010. Refer to study 17-M-0060.



ABOVE: NIMH director Dr. Joshua Gordon (l) gives a briefing on the BRAIN Initiative. At right, Congresswoman Rosa DeLauro (D-CT) and NIH director Dr. Francis Collins look through a magnifying glass at a microelectrode array used to record the activity of many neurons simultaneously from the living brain.

## House Delegation Visits NIH

PHOTOS: ERNIE BRANSON

House Labor, HHS and Education appropriations subcommittee chair Rep. Tom Cole (R-OK) led a visit to NIH of several members of the subcommittee and staff on Feb. 6 to tour laboratories and interact with researchers. In addition to Cole, the delegation included Rep. Andy Harris (R-MD), who is also a physician; Rep. Jaime Herrera Beutler (R-WA); Rep. John Moolenaar (R-MI); Rep. Rosa DeLauro (D-CT); Rep. Barbara Lee (D-CA); and Rep. Nita Lowey (D-NY).

Welcomed in the Clinical Research Center by NIH director Dr. Francis Collins, the group spent an afternoon in various meetings with NIH leadership, scientists and trainees. The visit included stops at the Porter Neuroscience Research Center for a tour of NIA's Laboratory of Neurogenetics and a conversation about the BRAIN Initiative with NINDS director Dr. Walter Koroshetz and NIMH director Dr. Joshua Gordon; NCI's Molecular



At left, Collins chats with Rep. Tom Cole (R-OK), chair of the House Labor, HHS and Education appropriations subcommittee, and Rep. Andy Harris (R-MD), who is also a physician. Cole led a delegation from Capitol Hill to tour NIH. At right, Congresswoman Barbara Lee (D-CA) talks with NIMHD director Dr. Eliseo Pérez-Stable (standing, c) and NCI acting director Dr. Doug Lowy.



Imaging Clinic for a briefing on cutting-edge prostate cancer diagnostics and treatment; and the metabolic unit for demonstrations of obesity-related exercise equipment and instrumentation.

Rounding out the visit, the congressional delegation sat down with several research fellows, postdocs and other trainees to hear firsthand about their NIH experiences.



ABOVE: Collins and NIH principal deputy director Dr. Lawrence Tabak join a number of research fellows, postdocs and other trainees who gave firsthand accounts of their NIH experiences.



The delegation stopped at the PNRC for a tour of NIA's Laboratory of Neurogenetics.